Application No. 09/667,489
Reply to Office Action dated December 23, 2003

REMARKS

Claims 1-9 were originally filed. Claims 5 and 7-9 are withdrawn from consideration as a result of the prior Restriction Requirement. Claims 1-4 and 6 are cancelled herein without prejudice or disclaimer to the subject matter recited therein. New Claims 10-35 are added herein. The new claims are fully supported by the specification as originally filed and do not constitute new matter. Accordingly, Applicants respectfully request entry of the above amendments to the claims and reconsideration of the claimed subject matter in light of the following remarks.

Final Restriction Requirement:

The Examiner acknowledged Applicants' election, with traverse, of Group II, Claims 1-4 and 6. However, the Examiner did not find Applicants' reasons for traversing to be persuasive and made the Restriction Requirement final. Accordingly, Claims 5 and 7-9 are withdrawn from consideration as being directed to non-elected subject matter. Applicants reserve the right to pursue the subject matter of these claims in separate divisional applications.

Priority:

The Examiner contends that the Applicants have not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120. In a telephone interview with the Examiner on January 12, 2004, the Examiner admitted that she had inadvertently read the Substitute Declaration that had accompanied the Request to Correct the Inventorship which was previously filed in the instant application as indicating that the instant application was a continuation application from a previously filed patent application. Since the instant application is **not** a continuation from the previously filed patent application, Applicants respectfully request that the objection to the application with respect to the priority claim be withdrawn.

Rejection of Claims 1-4 and 6 under 35 U.S.C. 102(b):

The Examiner has rejected Claims 1-4 and 6 under 35 U.S.C. 102(b) as being anticipated by the teachings of PCT Published Patent Application, WO 92/11046 ("Ahmad"). In particular, the Examiner contends that Ahmad discloses a dialysate solution for use in treating patients from kidney failure via dialysis treatment.

Claims 1-4 and 6 are cancelled herein, thereby rendering moot this rejection with respect to this claim. Applicants respectfully traverse this rejection with respect to new Claims 10-35 in light of the following remarks.

Hemodialysis is frequently performed with the systemic administration of an anti-coagulant to the patient in order to reduce and/or prevent coagulation of the patient's blood at the dialyzer membrane level. Coagulation of the patient's blood at the dialyzer membrane level results in a decrease in the transfer during dialysis of unwanted toxins and excess fluid from the patient's blood, which in turn increases the time in which it takes to normalize the patient's blood constituents during the dialysis process. Thus, by systemically administering an anticoagulant before or during hemodialysis, the coagulation at the dialyzer membrane level can be reduced or prevented. Unfortunately, there are those patients who require hemodialysis in the absence of a systemic administration of an anticoagulant or in the presence of a systemic administration of a low dose amount of an anticoagulant. Such patients include post-operative patents who undergo acute kidney failure due the kidneys' response to anesthesia. An anticoagulant should not be systemically administered to these patients because the patient's continued ability to clot blood is an important part of the healing process.

The instant invention is directed to the surprising discovery that hemodialysis performed with a dialysate composition of the invention resulted in a *localized* anti-coagulation effect at the point of the blood/dialysate interaction, *i.e.*, at the dialyzer membrane level. This is extremely beneficial to those patients who are unable to have an anticoagulant systemically administered prior to or during the hemodialysis procedure as discussed above and who are therefore at risk of having coagulation occur at the dialyzer membrane level during dialysis.

Another surprising discovery was that hemodialysis performed with a dialysate composition of the invention resulted in an observable increase in the reduction of urea in the patient's blood when compared with the reduction of blood urea in a patient undergoing hemodialysis with a dialysate composition that does not contain citrate. It also resulted in an observable increase in the concentration of bicarbonate in the patient's blood in comparison to the level of bicarbonate concentration obtained with a dialysate composition that does not contain citrate. This is extremely beneficial for those hemodialysis patients who suffer from chronic acidosis because the increased bicarbonate concentration will reduce the acidity of the patient's blood.

Accordingly, Applicants' invention, as reflected by new Claims 10-35, is the *method* of performing hemodialysis on a patient where the hemodialysis is performed *in the absence of systemic administration of an anti-coagulant* to the patent or *in the presence of a systemic administration of a low dose amount of an anticoagulant* and the dialysate composition contains *citrate at a concentration ranging from 2 mEq/L to 20 mEq/L* as the acidifying component of the dialysate (in contrast to the conventional use of acetic acid as the acidifying component of the dialysate composition) and *magnesium at a concentration ranging from 1 to 2 mEq/L*. The unexpected results of this method of performing hemodialysis is the *increased urea transfer* from the blood of the patent to the dialysate (as set forth in Claims 16 and 27), the *increased level of bicarbonate concentration in the patent's blood* (as set forth in Claims 17 and 28), the *increased effective flow of the patient's blood through the dialyzer* (as set forth in Claims 18 and 29) and the *increased re-use of the dialyzer* (as set forth in Claims 23 and 34).

In order to reject Claims 10-35 under 35 U.S.C. 102(b) in view of Ahmad for anticipation, the Examiner would have to demonstrate that each and every claim limitation is contained in the disclosure of Ahmad. See *Scripps Clinic & Research Foundation v. Genentech, Inc.*, 18 USPQ2nd 1001, 1010 (Fed Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 90 (Fed. Cir. 1986); see also MPEP § 2131 (August 2001). For the following reasons, Applicants respectfully submit that the disclosure of Ahmad fails to disclose all the limitations of the invention as set forth in new Claims 10-35 and therefore fails to anticipate these claims under 35 U.S.C. 102(b).

The disclosure of Ahmad is directed to dialysate compositions that, upon mixing with water, comprise the following:

from about 130 to about 150 mEq/L of sodium ion;

from about 0 to about 4.0 mEq/L of potassium ion;

from about 2.0 to about 3.5 mEq/L of calcium ion;

from about 0 to about 1.5 mEq/L of magnesium ion;

from about 25 to about 45 mEq/L of bicarbonate ion, acetate, lactate or combinations thereof;

from about 0 to about 2.0% glucose;

from about 90 to about 120 mEq/L of chloride ion;

and

from about 2 to about 12 mEq/L of citric acid.

Although Ahmad does disclose the use of above-described dialysate composition in hemodialysis of a patent with kidney failure, Ahmad does not disclose the use of the claimed dialysate composition *in the absence of systemic administration of an anticoagulant to the patient* or *in the presence of a systemic administration of a low dose amount of an anticoagulant.* Ahmad certainly does not disclose the use of the claimed dialysate composition *in the absence of systemic administration of an anticoagulant to the patient.* Furthermore, Ahmad fails to disclose the actual dialysate compositions utilized in new Claims 10-35. These dialysate compositions **require** the presence of magnesium. In contrast, the dialysate compositions disclosed in Ahmad optionally include magnesium (see, e.g., Claim 4 of Ahmad which states that magnesium is present at a concentration "from about 0 to about 1.5 mEq/L of magnesium ion"). The presence of magnesium and calcium in the claimed dialysate composition is essential in that it maintains the amount of magnesium and calcium present in the patient's blood at physiologically acceptable levels during the hemodialysis. Without the presence of magnesium and calcium in the dialysate composition, the citrate in the dialysate composition would bind to the free calcium and magnesium present in the patient's blood, which, in turn, would lower the amount of free calcium and magnesium in the patient's blood to potentially dangerous physiological levels. Thus, the presence of magnesium and calcium in the claimed dialysate composition is essential

in order to prevent physiological events that may occur as a result of low levels of magnesium and calcium in the blood of the patient undergoing hemodialysis.

In addition, Ahmad does not disclose the claimed dialysate compositions because the dialysate compositions disclosed in Ahmad can **not** contain citrate at a concentration level *greater* than 12 mEq/L.

In addition to the foregoing differences between Ahmad and the claimed subject matter, Ahmad fails to disclose the unexpected results achieved by the claimed method. In particular, Ahmad fails to disclose that the use of the claimed dialysate composition in hemodialysis would result in one or more of the following:

(1) an increased urea transfer from the patient's blood to the dialysate;
(2) an increased level of bicarbonate concentration in the patient's blood;
(3) an increased effective flow of the patient's blood through the dialyzer; or
(4) an increased re-use of the dialyzer.

Without some disclosure in Ahmad of the possibility of these results, one of ordinary skill in the art would not reasonably expect that hemodialysis performed with a Ahmad dialysate composition would produce such results, especially when one considers that the dialysate compositions disclosed in Ahmad do not require the presence of magnesium, which is an essential component of the dialysate compositions utilized in the instant invention.

In view of the fact that Ahmad fails to disclose the claimed dialysate compositions used in new Claims 10-35, in view of the fact that Ahmad fails to disclose the unexpected results of the claimed invention, and in view of the fact that Ahmad fails to disclose a method of performing hemodialysis on a patient in the absence of systemic administration of an anticoagulant to the patient, Applicants respectfully submit that Ahmad fails to anticipate new Claims 10-34. Accordingly, Applicants respectfully submit that new Claims 10-35 are patentable under 35 U.S.C. 102(b) in light of the teachings of Ahmad. Favorable consideration and early allowance is respectfully requested.

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The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,

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